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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.				
10/525,259	02/22/2005	Margaret Sin Ka Wan	13404US	5000				
7590 Battelle Memorial Institute 505 King Avenue Columbus, OH 43201-2693		10/12/2007	<table border="1"><tr><td colspan="2">EXAMINER</td></tr><tr><td colspan="2">FERNANDEZ, SUSAN EMILY</td></tr></table>		EXAMINER		FERNANDEZ, SUSAN EMILY	
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Please find below and/or attached an Office communication concerning this application or proceeding.

The time period for reply, if any, is set in the attached communication.

Office Action Summary	Application No. 10/525,259	Applicant(s) WAN, MARGARET SIN KA	
	Examiner Susan E. Fernandez	Art Unit 1651	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

- 1) ☒ Responsive to communication(s) filed on 18 June 2007.
- 2a) ☒ This action is **FINAL**. 2b) ☐ This action is non-final.
- 3) ☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

- 4) ☒ Claim(s) 1-30,35,36 and 49-53 is/are pending in the application.
- 4a) Of the above claim(s) _____ is/are withdrawn from consideration.
- 5) ☐ Claim(s) _____ is/are allowed.
- 6) ☒ Claim(s) 1-30,35,36 and 49-53 is/are rejected.
- 7) ☐ Claim(s) _____ is/are objected to.
- 8) ☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

- 9) ☐ The specification is objected to by the Examiner.
- 10) ☐ The drawing(s) filed on _____ is/are: a) ☐ accepted or b) ☐ objected to by the Examiner.
Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).
Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).
- 11) ☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

- 12) ☒ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).
- a) ☒ All b) ☐ Some * c) ☐ None of:
- ☐ Certified copies of the priority documents have been received.
 - ☐ Certified copies of the priority documents have been received in Application No. _____.
 - ☒ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

- | | |
|--|---|
| 1) <input type="checkbox"/> Notice of References Cited (PTO-892) | 4) <input type="checkbox"/> Interview Summary (PTO-413)
Paper No(s)/Mail Date. _____ |
| 2) <input type="checkbox"/> Notice of Draftsperson's Patent Drawing Review (PTO-948) | 5) <input type="checkbox"/> Notice of Informal Patent Application |
| 3) <input type="checkbox"/> Information Disclosure Statement(s) (PTO/SB/08)
Paper No(s)/Mail Date _____ | 6) <input type="checkbox"/> Other: _____ |

DETAILED ACTION

The amendment filed June 18, 2007, has been received and entered.

Claims 31-34 and 37-48 are cancelled. Claims 52 and 53 are new.

Claims 1-30, 35, 36, and 49-53 are pending and examined on the merits to the extent they read on the elected invention.

Claim Rejections - 35 USC § 112

The following is a quotation of the second paragraph of 35 U.S.C. 112:

The specification shall conclude with one or more claims particularly pointing out and distinctly claiming the subject matter which the applicant regards as his invention.

Claims 52 and 53 are rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention.

Claims 52 and 53 are rendered indefinite by the recitation "the target" since it lacks antecedent basis. It is suggested that "the target" be replaced with "the target area."

Claim Rejections - 35 USC § 103

The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

(a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negated by the manner in which the invention was made.

Claims 1-18, 20-28, 35, 36, and 49-53 are rejected under 35 U.S.C. 103(a) as being unpatentable over Coffee et al. (WO 98/03267) in view of Shastri et al. (WO 97/16545).

Coffee et al. discloses a method of depositing fibres on a surface wherein a liquid comprising a biocompatible polymer is subjected to an electrohydrodynamic process in the vicinity of said surface (page 4, third paragraph). See Figure 1. Thus, Coffee et al. discloses supplying liquid comprising compatible polymer to a liquid outlet in the vicinity of a surface and subjecting liquid issuing from the outlet to an electric field to cause the liquid to form polymer fibres which are attracted to and deposit onto the surface to form a polymer fibre scaffold, as required by certain limitations in parent claims 1, 14, 16, 18, 20, 21, and 24. Given that the Coffee method can be used to form a mat or web of fibres (page 21, last paragraph, and Figure 9), Coffee et al. teaches the creation of a three-dimensional continuous network of intercommunicating fibre portions.

Additionally, the reference teaches that the fibres can have a diameter in the range of 10 nm to above 100 microns (page 17, first paragraph, second to last sentence), which meets the diameter limitation of instant claim 7. Further still, the reference teaches that the liquid comprising a biocompatible polymer can be a solution or a melt (page 22, last paragraph) and the polymer can be polylactic acid (polylactide) (page 4, second paragraph) or "New Skin" wherein the fibres formed are approximately 0.5 to 5 microns in diameter (page 19, last paragraph). Thus, limitations in instant claims 10, 22, and 23 are disclosed in the reference. Additionally, the limitations of instant claims 25, 26, 49, 52, and 53 are taught by Coffee et al. (page 4, second paragraph and third paragraph).

Coffee et al. differs from the claimed invention in that it does not expressly disclose that mammalian cells are applied to the Coffee polymer fibre scaffold.

Shastri et al. discloses a method for altering the regeneration, differentiation, or function of cells (claim 1), wherein cells are attached to a surface comprising an electrically conducting polymer (such as a biocompatible polymer, see claim 10). See also the abstract which indicates that conductive polymers are seeded with nerve cells. As indicated at page 15, lines 13-19, the electrically conducting polymer should be porous, where the pores should allow for vascular ingrowth and the seeding of cells without damage to the cells or patient, said pores generally in the range of between approximately 100 and 300 microns. Further still, the Shastri invention can be used to alter the regeneration, differentiation, or function of cells including various "organ cells", muscles cells, and "cells forming bone and cartilage" (page 18, lines 24-27).

At the time the invention was made, it would have been obvious to a person of ordinary skill in the art to have applied mammalian cells to the fibre scaffold produced by the Coffee methods. One of ordinary skill in the art would have been motivated to do this since the Coffee scaffold comprises of electrically conducting polymer and therefore would have been suitable for cell regeneration and differentiation. In applying mammalian cells either by spraying or seeding (as suggested in Shastri et al.), the applied cells would have inherently grown or elongated preferentially along the fibre of the Coffee fibre scaffold. Thus, claim 1 and its dependants as discussed above (claims 1, 7, 10, 22, 23, 27, 28, and 49) are rendered obvious.

Given that Shastri et al. teaches that the attachment of various types of cells can be used to alter the regeneration, differentiation, or function of cells, it would have been obvious that the regeneration, differentiation, or function of any type of cells, including human adherent cells, human fibroblast cells, and stem cells, would have been altered when applied to the Coffee

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scaffold. Thus, the cell types recited in claims 11-14 and 16-18 (and the preamble of parent claims 1, 14, 16, 18, 20, 21, and 24) are rendered obvious.

Given the variety of cells that may be applied to the Coffee invention, a wide range of cell sizes would have been applied. Therefore, the diameter of the cells applied could fit within the requirements recited in instant claims 2-6, 8, and 9. Claims 2-6, 8, and 9 are thus rendered obvious.

It is further pointed out that it would have been obvious to a person of ordinary skill in the art to have varied the gap distance between the fibres in the Coffee scaffold to other gap distances, including those recited in the instant claims, through routine experimentation since pores influence the degree of cellular growth. Shastri et al. teaches that pore sizes of about 100 to 300 microns are suitable for their purposes, thus it would have been obvious that gap distances of 100 to 300 microns would have been suitable in the Coffee invention for cellular regeneration, differentiation, and function. Thus, the gap distance limitations in instant claims 15, 18, 20, 21, 24, 35, and 36 are rendered obvious.

In sum, claims 1-18, 20-28, 35, 36, and 49-53 are rendered obvious by the references.

Claims 1-30, 35, 36, and 49-53 are rejected under 35 U.S.C. 103(a) as being unpatentable over Coffee et al. and Shastri et al. as applied to claims 1-18, 20-28, 35, 36, and 49-53 above, and further in view of Smith et al. (WO 01/27365) and Simpson et al. (WO 02/40242).

As discussed above, Coffee et al. and Shastri et al. render claims 1-18, 20-28, 35, 36, and 49-53 obvious. However, these references do not expressly disclose that the polymer used is polycaprolactone.

Smith et al. discloses that polycaprolactone is a polymer suitable for making fiber wherein a polymer solution in a liquid jet is introduced into an electric field and formed and elongated on a surface, such as a wound (page 11, lines 4-6, page 14, lines 17-20, and page 17, lines 14-20).

At the time the invention was made, it would have been obvious to a person of ordinary skill in the art to have created the fibre scaffold rendered obvious by Coffee et al. and Shastri et al. with a solution comprising polycaprolactone. One of ordinary skill in the art would have been motivated to do this since polycaprolactone is a polymer which can form fibres on a surface when exposed to an electric field and can be used in a wound dressing, as required by Coffee et al. Thus, further limitations of claims 10 and 14, and claim 19 are rendered obvious by the references.

Additionally, Coffee et al. and Shastri et al. differ from the claimed invention in that they do not teach preparing a liquid formulation comprising cell culture medium with a water soluble polymer, or that this liquid formulation is exposed to an electric field to cause the liquid to break into droplets or to form at least one fibre.

Simpson et al. discloses using mixed solutions (nonbiological but biologically compatible material along with substances such as cells) in electroprocessing, wherein fibres or droplets are formed composed of electroprocessed materials as well as one or more substances (page 33, lines 25-28). Electroprocessing is streaming, spraying, sputtering or dripping material across an electric field and toward a target (page 6, lines 37-40).

At the time the invention was made, it would have been obvious to a person of ordinary skill in the art to have introduced mammalian cells by combining a cell culture with a polymer

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for the formation of fibres by electroprocessing when conducting the invention rendered obvious by Coffee et al. and Shastri et al. One of ordinary skill in the art would have been motivated to do this since this technique is appropriate for delivering cells to an electroprocessed polymer and further would allow formation of fibres as required by Coffee et al. Thus, claims 29 and 30 are rendered obvious.

Note further that Simpson et al. provides further motivation for applying mammalian cells to the Coffee scaffold as Simpson et al. teaches combining cells with an electroprocessed collagen matrix in order to provide scaffolding or seeding for the formation of engineered tissue, where the cells include stems cells and fibroblasts (page 17, lines 19-32 and abstract).

A holding of obviousness is clearly required.

Response to Arguments

Applicant's arguments filed June 18, 2007, have been fully considered but they are not persuasive. Though Coffee et al. does not state that the fibre diameter should have a size relative to a diameter of the mammalian cells so as to facilitate at least one cell process as set out in instant claim 1, Coffee et al. indeed discloses that the fibre diameter is from 1 to 12 microns, as recited in claim 7, and therefore meets the fibre diameter recitation recited in claim 1. As discussed in the previous office action, the limitations in the claims regarding the gaps between the fibre portions are rendered obvious by combining Coffee et al. with Shastri et al.

In regards to Shastri et al., the applicant indicates that Shastri et al. teaches that a scaffold should be of material other than the electrically conducting polymer it discloses for practice of its invention. The applicant cites page 40, lines 31 and 32, and page 50, lines 29-32. However,

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there are only 29 pages in the Shastri reference, thus the support for the assertions made by the applicant is unclear. Applicant also argues that “by describing many different physical forms including thin films, laminates, and coatings for the electrically conducting polymer, Shastri et al. teaches that the physical form of the polymer is not important...” However, it is respectfully noted that Shastri et al. indicates at page 15, lines 13-19 that for vascular ingrowth, the matrix should be a porous template.

Though Shastri et al. does not disclose subjecting liquid issuing from an outlet to an electric field to cause the liquid to form polymer fibre which is attracted to and deposits onto a surface to form a polymer fibre scaffold comprising a three-dimensional continuous network of intercommunicating fibre portions, it is respectfully noted that the primary reference, Coffee et al., teaches this embodiment (Coffee et al., page 21, last paragraph). Shastri et al. provides motivation to apply cells to the Coffee polymer fibre scaffold. Moreover, as discussed in the previous office action, it would have been obvious to a person of ordinary skill in the art to have varied the gap distance between the fibres in the Coffee scaffold to other gap distances, including those recited in the instant claims, through routine experimentation since the pores influence the degree of cellular growth. Applicant asserts that the references do not attach any importance to the fibre diameter and the fibre gap size. However, it is respectfully noted that Coffee et al. indeed teaches fibre diameters recited in the claims, and that Shastri et al. recognizes the importance of fibre gap size by indicating that pores in a matrix should allow vascular ingrowth and the seeding of cells without damage to the cells or patient.

It is respectfully noted that Shastri et al. indicates that the attachment of various cell types can be used to alter the regeneration, differentiation, or function of cells, thus it would have been

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obvious the regeneration, differentiation, or function of any type of cell, including those recited in the claims (for instance, claim 18).

In response to applicant's argument that the examiner's conclusion of obviousness is based upon improper hindsight reasoning, it must be recognized that any judgment on obviousness is in a sense necessarily a reconstruction based upon hindsight reasoning. But so long as it takes into account only knowledge which was within the level of ordinary skill at the time the claimed invention was made, and does not include knowledge gleaned only from the applicant's disclosure, such a reconstruction is proper. See *In re McLaughlin*, 443 F.2d 1392, 170 USPQ 209 (CCPA 1971).

In response to applicant's arguments against the references individually, one cannot show nonobviousness by attacking references individually where the rejections are based on combinations of references. See *In re Keller*, 642 F.2d 413, 208 USPQ 871 (CCPA 1981); *In re Merck & Co.*, 800 F.2d 1091, 231 USPQ 375 (Fed. Cir. 1986).

As discussed above, Coffee et al. indeed teaches a polymer fibre which is attracted to and deposits onto a surface to form a polymer fibre scaffold comprising a three-dimensional continuous network of intercommunicating fibre portions having a given fibre diameter. It is through combination of Coffee et al. with Shastri et al. that the gap distances are rendered obvious. Thus, the combination of Coffee et al. with Shastri et al. renders the claimed invention obvious, as does the combination of these two references with Simpson et al.

No claims are allowed.

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Applicant's amendment necessitated the new ground(s) of rejection presented in this Office action. Accordingly, **THIS ACTION IS MADE FINAL**. See MPEP § 706.07(a).

Applicant is reminded of the extension of time policy as set forth in 37 CFR 1.136(a).

A shortened statutory period for reply to this final action is set to expire **THREE MONTHS** from the mailing date of this action. In the event a first reply is filed within **TWO MONTHS** of the mailing date of this final action and the advisory action is not mailed until after the end of the **THREE-MONTH** shortened statutory period, then the shortened statutory period will expire on the date the advisory action is mailed, and any extension fee pursuant to 37 CFR 1.136(a) will be calculated from the mailing date of the advisory action. In no event, however, will the statutory period for reply expire later than **SIX MONTHS** from the date of this final action.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Susan E. Fernandez whose telephone number is (571) 272-3444. The examiner can normally be reached on Mon-Fri 8:30 am - 5:00 pm.

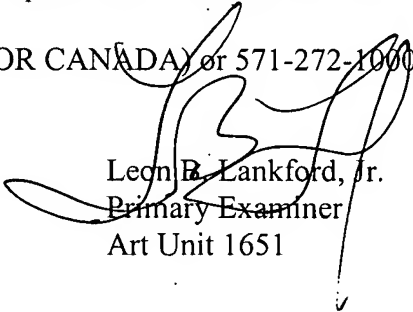
If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Mike Wityshyn can be reached on (571) 272-0926. The fax phone number for the organization where this application or proceeding is assigned is 571-273-8300.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR

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system, see <http://pair-direct.uspto.gov>. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free). If you would like assistance from a USPTO Customer Service Representative or access to the automated information system, call 800-786-9199 (IN USA OR CANADA) or 571-272-1000.

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sef